AMENDMENT

It is respectfully requested that the application be amended, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as follows:

IN THE CLAIMS:

1-19 (Cancelled).

20. (Original) A diagnostic method comprising determining the sequence of an acquired immunodeficiency virus envelope gene V3 region before initiating antiretroviral therapy to determine a suitable antiretroviral treatment regimen.

21. (Original) The diagnostic method according to claim 20, wherein the envelope gene encodes gp160 or gp120.

22. (Original) The diagnostic method according to claim 20, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

23. (Original) The diagnostic method according to claim 20, wherein the antiretroviral therapy is selected from the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, 3TC, AZT, nevirapine, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors.

24. (Original) A diagnostic method comprising determining the sequence of an acquired immunodeficiency virus envelope gene V3 region after initiating antiretroviral therapy to monitor efficacy of a antiretroviral treatment regimen and where efficacy of the treatment is directly related to decrease of CXCR4 coreceptor use.

25. (Original) The diagnostic method according to claim 24, wherein the envelope gene encodes gp160 or gp120.

26. (Original) The diagnostic method according to claim 24, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

27. (Original) The diagnostic method according to claim 24, wherein the antiretroviral therapy is selected from the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, 3TC, AZT, nevirapine, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors.

28. (Original) The diagnostic method according to claim 20, wherein the sequence of the envelope gene V3 region is determined from a DNA micro-chip array.

29. (Original) The diagnostic method according to claim 24, wherein the sequence of the envelope gene V3 region is determined from a DNA micro-chip array.

30. (Original) A diagnostic method comprising determining CXCR4 coreceptor use, CCR5 coreceptor use, and a ratio of acquired immunodeficiency virus using the CXCR4 coreceptor compared to virus using the CCR5 coreceptor.

31. (Original) A diagnostic method comprising determining CXCR4 coreceptor use, CCR5 coreceptor use, and a ratio of acquired immunodeficiency virus using the CXCR4 coreceptor compared to virus using the CCR5 coreceptor before initiating antiretroviral therapy to determine a suitable antiretroviral treatment regimen.

32. (Original) A diagnostic method comprising determining CXCR4 coreceptor use, CCR5 coreceptor use, and a ratio of acquired immunodeficiency virus using the CXCR4 coreceptor compared to virus using the CCR5 coreceptor after initiating antiretroviral therapy to monitor efficacy of an antiretroviral treatment regimen and where efficacy of the treatment is directly related to decrease of CXCR4 coreceptor use.

33. (Original) A diagnostic method comprising transforming cells with an HIV envelope gene variant cloned from a patient infected with HIV, selectively fusing the cells with an indicator cell line expressing an HIV envelope-compatible coreceptor, and assaying for cell fusion before initiating antiretroviral therapy to determine a suitable antiretroviral treatment regimen.

34. (Original) The diagnostic method according to claim 33, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

35. (Original) The diagnostic method according to claim 33, wherein the antiretroviral therapy is selected from the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, 3TC, AZT, nevirapine, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors.

36. (Original) A diagnostic method comprising transforming cells containing a selectively activatable reporter gene construct with an HIV envelope gene variant cloned from a patient infected with HIV, selectively fusing the cells with an indicator cell line containing a constitutively active transcriptional activator of the reporter gene construct and an HIV envelope-compatible coreceptor, and assaying for fusion by detection of reporter gene expression before initiating antiretroviral therapy to determine a suitable antiretroviral treatment regimen.

37. (Original) The diagnostic method according to claim 36, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

38. (Original) The diagnostic method according to claim 36, wherein the antiretroviral therapy is selected from the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, 3TC, AZT, nevirapine, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors.

39. (Original) A diagnostic method comprising transforming cells containing an HIV Tat-activatable reporter gene construct with an HIV envelope gene variant cloned from a patient infected with HIV, selectively fusing the cells with an indicator cell line containing a constitutively active *tat* gene and an HIV envelope-compatible coreceptor, and assaying for fusion by detection of reporter gene expression before initiating antiretroviral therapy to determine a suitable antiretroviral treatment regimen.

40. (Original) The diagnostic method according to claim 39 wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

41. (Original) The diagnostic method according to claim 39, wherein the antiretroviral therapy is selected from the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, 3TC, AZT, nevirapine, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors.

42. (Original) A diagnostic method comprising transforming cells with an HIV envelope gene variant cloned from a patient infected with HIV, selectively fusing the cells with an indicator cell line expressing an HIV envelope-compatible coreceptor, and assaying for cell fusion after initiating antiretroviral therapy to monitor efficacy of an antiretroviral treatment regimen and where efficacy of the treatment is directly related to decrease of CXCR4 coreceptor use.

43. (Original) The diagnostic method according to claim 42, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

44. (Original) The diagnostic method according to claim 42, wherein the antiretroviral therapy is selected from the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, 3TC, AZT, nevirapine, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors.

45. (Original) A diagnostic method comprising transforming cells containing a selectively activatable reporter gene construct with an HIV envelope gene variant cloned from a patient infected with HIV, selectively fusing the cells with an indicator cell line containing a constitutively active transcriptional activator of the reporter gene construct and an HIV envelope-compatible coreceptor, and assaying for fusion by detection of reporter gene expression after initiating antiretroviral therapy to monitor efficacy of an antiretroviral treatment regimen and where efficacy of the treatment is directly related to decrease of CXCR4 coreceptor use.

46. (Original) The diagnostic method according to claim 45, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

47. (Original) The diagnostic method according to claim 45, wherein the antiretroviral therapy is selected from the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, 3TC, AZT, nevirapine, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors.

48. (Original) A diagnostic method comprising transforming cells containing an HIV Tat-activatable reporter gene construct with an HIV envelope gene variant cloned from a patient infected with HIV, selectively fusing the cells with an indicator cell line containing a constitutively active *tat* gene and an HIV envelope-compatible coreceptor, and assaying for fusion by detection of reporter gene expression after initiating antiretroviral therapy to monitor efficacy of an antiretroviral treatment regimen and where efficacy of the treatment is directly related to decrease of CXCR4 coreceptor use.

49. (Previously Presented) The diagnostic method according to claim 48, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

50. (Previously Presented) The diagnostic method according to claim 48, wherein the antiretroviral therapy is selected from the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, 3TC, AZT, nevirapine, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors.

51. (Original) A diagnostic composition comprising one or more cells comprising an HIV Tat-activatable reporter gene construct, an HIV envelope gene variant cloned from an infected patient, a constitutively active *tat* gene and an HIV envelope-compatible coreceptor.

52. (Original) The composition according to claim 51, wherein the coreceptor is CXCR4.

53. (Original) The composition according to claim 51, wherein the coreceptor is CCR5.

54. (Previously Presented) A method of monitoring the efficacy of antiretroviral therapy in a patient comprising quantitating usage of the CXCR4 and/or CCR5 coreceptor in a patient-derived acquired immunodeficiency virus primary isolate, and determining whether there has been a shift back in coreceptor usage from the CXCR4 to the CCR5 coreceptor, whereby a shift back towards CCR5 coreceptor usage indicates that the antiretroviral therapy is effective.

55. (Previously Presented) The diagnostic method according to claim 54, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

56. (Previously Presented) The method according to claim 54, wherein quantitating the population of virus using the CXCR4 and CCR5 coreceptor comprises determining the ratio of virus using the CXCR4 coreceptor compared to virus using the CCR5 coreceptor.

57. (Previously Presented) The method according to claim 54, where in the patient-derived acquired immunodeficiency virus sample is obtained from peripheral blood.

58. (Previously Presented) The method according to claim 54, where in the patient-derived acquired immunodeficiency virus sample is obtained from genital secretions.

59. (Previously Presented) The method according to claim 54, where in the patient-derived acquired immunodeficiency virus sample is obtained from cerebrospinal fluid.

60. (Previously Presented) A method of determining CXCR4 and/or CCR5 coreceptor usage in a patient before initiating antiretroviral therapy, comprising obtaining patient-derived acquired immunodeficiency virus and quantitating usage of the CXCR4 and/or CCR5 coreceptor in a patient-derived acquired immunodeficiency virus primary isolate, whereby the CXCR4 and/or CCR5 coreceptor usage of the patient is used to determine a suitable antiretroviral treatment regimen.

61. (Previously Presented) The diagnostic method according to claim 60, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

62. (Previously Presented) The diagnostic method according to claim 60, wherein the antiretroviral therapy is selected from the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors.

63. (Previously Presented) The method according to claim 60, where in the patient-derived acquired immunodeficiency virus sample is obtained from peripheral blood.

64. (Previously Presented) The method according to claim 60, where in the patient-derived acquired immunodeficiency virus sample is obtained from genital secretions.

65. (Previously Presented) The method according to claim 60, where in the patient-derived acquired immunodeficiency virus sample is obtained from cerebrospinal fluid.

66. (Previously Presented) A method of monitoring the efficacy of antiretroviral therapy in a patient comprising obtaining patient-derived acquired immunodeficiency virus samples before and after initiating antiretroviral therapy and quantitating usage of the CXCR4 and/or CCR5 coreceptor in a patient-derived acquired immunodeficiency virus sample, whereby a decrease of CXCR4 coreceptor use after initiating antiretroviral therapy indicates that the antiretroviral therapy is effective.

67. (Previously Presented) The diagnostic method according to claim 66, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

68. (Previously Presented) The diagnostic method according to claim 66, wherein the antiretroviral therapy is selected from the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors.

69. (Previously Presented) The method according to claim 66, where in the patient-derived acquired immunodeficiency virus sample is obtained from peripheral blood.

70. (Previously Presented) The method according to claim 66, where in the patient-derived acquired immunodeficiency virus sample is obtained from genital secretions.

71. (Previously Presented) The method according to claim 66, where in the patient-derived acquired immunodeficiency virus sample is obtained from cerebrospinal fluid.

72. (Previously Presented) A method of determining CXCR4 and/or CCR5 coreceptor usage in a patient-derived acquired immunodeficiency virus sample comprising determining CXCR4 and CCR5 coreceptor use the sample, and determing a ratio of acquired immunodeficiency virus using the CXCR4 coreceptor compared to virus using the CCR5 coreceptor.

73. (Previously Presented) The method according to claim 72, where in the patient-derived acquired immunodeficiency virus sample is obtained from peripheral blood.

74. (Previously Presented) The method according to claim 72, where in the patient-derived acquired immunodeficiency virus sample is obtained from genital secretions.

75. (Previously Presented) The method according to claim 72, where in the patient-derived acquired immunodeficiency virus sample is obtained from cerebrospinal fluid.

76. (Previously Presented) A method of determining the ratio of CXCR4 to CCR5 coreceptor usage in a patient-derived acquired immunodeficiency virus sample before initiating antiretroviral therapy comprising determining CXCR4 and CCR5 coreceptor use in the sample, and determining the ratio of acquired immunodeficiency virus using the CXCR4 coreceptor compared to virus using the CCR5 coreceptor before initiating antiretroviral therapy, whereby the ratio of CXCR4 to CCR5 coreceptor usage is used to determine a suitable antiretroviral treatment regimen.

77. (Previously Presented) The method according to claim 76, where in the patient-derived acquired immunodeficiency virus sample is obtained from peripheral blood.

78. (Previously Presented) The method according to claim 76, where in the patient-derived acquired immunodeficiency virus sample is obtained from genital secretions.

79. (Previously Presented) The method according to claim 76, where in the patient-derived acquired immunodeficiency virus sample is obtained from cerebrospinal fluid.

80. (Previously Presented) A method of monitoring the efficacy of antiretroviral therapy in a patient comprising determining CXCR4 and CCR5 coreceptor use in patient-derived acquired immunodeficiency virus samples, and determining the ratio of acquired

immunodeficiency virus using the CXCR4 coreceptor compared to virus using the CCR5 coreceptor after initiating antiretroviral whereby efficacy of the antiretroviral therapy is directly related to a decrease of CXCR4 coreceptor use after initiation of the therapy.

81. (Previously Presented) The method according to claim 80, where in the patient-derived acquired immunodeficiency virus sample is obtained from peripheral blood.

82. (Previously Presented) The method according to claim 80, where in the patient-derived acquired immunodeficiency virus sample is obtained from genital secretions.

83. (Previously Presented) The method according to claim 80, where in the patient-derived acquired immunodeficiency virus sample is obtained from cerebrospinal fluid.

84. (Previously Presented) A method of monitoring the efficacy of antiretroviral therapy in a patient comprising the steps of:

a) obtaining a first patient-derived acquired immunodeficiency virus sample either before or after the initiation of antiretroviral therapy;

b) assaying the first patient-derived acquired immunodeficiency virus sample for CXCR4 and CCR5 coreceptor use;

c) determining the ratio of virus in the first patient-derived acquired immunodeficiency virus sample using the CXCR4 coreceptor compared to virus using the CCR5 coreceptor;

d) obtaining a second patient-derived acquired immunodeficiency virus sample at a time subsequent to the initiation of antiretroviral therapy and subsequent to the time at which the first sample is obtained;

e) repeating steps b) through d) with the second sample;

f) determining whether there is a difference in the ratio of CXCR4 and CCR5 coreceptor usage between the first and second patient-derived acquired immunodeficiency virus samples,

whereby a increase in the ratio of CCR5 coreceptor usage, or a decrease in the ratio of CXCR4 coreceptor in the second sample as compared to the first sample, indicates that the antiretroviral therapy is effective.

85. (Previously Presented) The method according to claim 84, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

86. (Previously Presented) The method according to claim 84, where in the patient-derived acquired immunodeficiency virus sample is obtained from peripheral blood.

87. (Previously Presented) The method according to claim 84, where in the patient-derived acquired immunodeficiency virus sample is obtained from genital secretions.

88. (Previously Presented) The method according to claim 84, where in the patient-derived acquired immunodeficiency virus sample is obtained from cerebrospinal fluid.

89. (Previously Presented) The method according to claim 84 wherein the antiretroviral therapy is selected from the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors.

90. (Previously Presented) The method according to claim 89, wherein the nucleoside analogue reverse transcriptase inhibitor is 3TC.

91. (Previously Presented) The method according to claim 89, wherein the nucleoside analogue reverse transcriptase inhibitor is AZT.

92. (Previously Presented) The method according to claim 89, wherein the non-nucleoside analogue reverse transcriptase inhibitor is nevirapine.

93. (Previously Presented) A method of monitoring the efficacy of antiretroviral therapy in a patient comprising the steps of:

a) obtaining a first patient-derived acquired immunodeficiency virus sample either before or after the initiation of antiretroviral therapy;

b) assaying the first patient-derived acquired immunodeficiency virus sample for CXCR4 and CCR5 coreceptor use;

c) determining the ratio of virus in the first patient-derived acquired immunodeficiency virus sample using the CXCR4 coreceptor compared to virus using the CCR5 coreceptor;

d) obtaining a second patient-derived acquired immunodeficiency virus sample at a time subsequent to the initiation of antiretroviral therapy and subsequent to the time at which the first sample is obtained;

e) repeating steps b) through d) with the second sample;

f) determining whether there is a difference in the ratio of CXCR4 and CCR5 coreceptor usage between the first and second patient-derived acquired immunodeficiency virus samples,

whereby a decrease in the ratio of CCR5 coreceptor usage, or an increase in the ratio of CXCR4 coreceptor in the second sample as compared to the first sample, indicates that the antiretroviral therapy is not effective.

94. (Previously Presented) The method according to claim 93, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

95. (Previously Presented) The method according to claim 93, where in the patient-derived acquired immunodeficiency virus sample is obtained from peripheral blood.

96. (Previously Presented) The method according to claim 93, where in the patient-derived acquired immunodeficiency virus sample is obtained from genital secretions.

97. (Previously Presented) The method according to claim 93, where in the patient-derived acquired immunodeficiency virus sample is obtained from cerebrospinal fluid.

98. (Previously Presented) The method according to claim 93, wherein the antiretroviral therapy is selected from the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors.

99. (Previously Presented) The method according to claim 98, wherein the nucleoside analogue reverse transcriptase inhibitor is 3TC.

100. (Previously Presented) The method according to claim 98, wherein the nucleoside analogue reverse transcriptase inhibitor is AZT.

101. (Previously Presented) The method according to claim 98, wherein the non-nucleoside analogue reverse transcriptase inhibitor is nevirapine.

102. (Previously Presented) A method of monitoring the efficacy of antiretroviral therapy in a patient comprising the steps of:

a) obtaining a first patient-derived acquired immunodeficiency virus sample either before or after the initiation of antiretroviral therapy;

b) assaying the first patient-derived acquired immunodeficiency virus sample for CXCR4 or CCR5 coreceptor use;

c) determining the ratio of virus in the first patient-derived acquired immunodeficiency virus sample using the CXCR4 coreceptor compared to virus using the CCR5 coreceptor;

d) obtaining a second patient-derived acquired immunodeficiency virus sample at a time subsequent to the initiation of antiretroviral therapy and subsequent to the time at which the first sample is obtained;

e) repeating steps b) through d) with the second sample;

f) determining whether there is a difference in the ratio of CXCR4 and CCR5 coreceptor usage between the first and second patient-derived acquired immunodeficiency virus samples,

whereby the lack of a difference in the ratio of CCR5 coreceptor usage, or the lack of a difference in the ratio of CXCR4 coreceptor usage, between the first and second patient derived virus samples, indicates that the antiretroviral therapy is not effective.

103. (Previously Presented) The method according to claim 102, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

104. (Previously Presented) The method according to claim 102, where in the patient-derived acquired immunodeficiency virus sample is obtained from peripheral blood.

105. (Previously Presented) The method according to claim 102, where in the patient-derived acquired immunodeficiency virus sample is obtained from genital secretions.

106. (Previously Presented) The method according to claim 102, where in the patient-derived acquired immunodeficiency virus sample is obtained from cerebrospinal fluid.

107. (Previously Presented) The method according to claim 102, wherein the antiretroviral therapy is selected from the group consisting of highly active antiretroviral therapy (HAART), protease inhibitors, fusion inhibitors, integrase inhibitors, coreceptor specific agents, non-nucleoside analogue reverse transcriptase inhibitors and nucleoside analogue reverse transcriptase inhibitors.

108. (Previously Presented) The method according to claim 107, wherein the nucleoside analogue reverse transcriptase inhibitor is 3TC.

109. (Previously Presented) The method according to claim 107, wherein the nucleoside analogue reverse transcriptase inhibitor is AZT.

110. (Previously Presented) The method according to claim 107, wherein the non-nucleoside analogue reverse transcriptase inhibitor is nevirapine.

111. (New) A method of monitoring the efficacy of antiretroviral therapy in a patient comprising quantitating usage of CXCR4 and/or CCR5 coreceptors in a patient-derived acquired immunodeficiency virus population from the patient, whereby a shift towards CCR5 coreceptor usage indicates that the antiretroviral therapy is effective.

112. (New) The method according to claim 111, wherein the acquired immunodeficiency virus is selected from the group consisting of HIV-1 and HIV-2.

113. (New) The method according to claim 111, wherein quantitating the population of virus using the CXCR4 and CCR5 coreceptor comprises determining the ratio of virus using the CXCR4 coreceptor compared to virus using the CCR5 coreceptor.

114. (New) The method according to claim 111, where in the patient-derived acquired immunodeficiency virus sample is obtained from peripheral blood.

115. (New) The method according to claim 111, where in the patient-derived acquired immunodeficiency virus sample is obtained from genital secretions.

116. (New) The method according to claim 111, where in the patient-derived acquired immunodeficiency virus sample is obtained from cerebrospinal fluid.